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LEPTOSPIROSIS - A DISEASE ENDEMIC TO SOUTHERN LOUISIANA - Part II

BY

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CLINICAL FEATURES

The incubation period of leptospirosis varies from 3 to 20 days. This incubation period generally does not vary significantly among serotypes and is of no prognostic importance.

The clinical course of anicteric leptospiral infection is biphasic.[1,2] The initial or "septicemic phase" is characterized by development of an acute systemic infection, with sudden onset, high fever, frequently accompanied by chills, marked prostration, headache, and severe muscle aching. Fever persists on a high level for 7 to 10 days, after which it drops to normal and remains so for 2 to 5 days. It is then followed by a more moderate rise subsiding into a long sub-febrile period. Physical findings during the septicemic stage are often nonspecific. In addition to fever, dehydration, irritability, muscle tenderness, conjunctival suffusion, and a variety of skin rashes are commonly noted. Not infrequently the mucous membranes are red and swollen. The patient, during the initial phase of the disease, characteristically lies apathetic and motionless in a recumbent position, whining during the febrile period because of severe headaches, myalgia, and joint pains. Most affected are the muscles of the calves, abdomen, back, and chest. Local pressure is very painful.

The second or "immune phase" is more variable in its symptomatology than the septicemic stage and typically follows an afebrile and relatively asymptomatic period of 1 to 3 days duration. Leptospires are found only in renal or ocular tissue during this stage, where previously the disease organisms could be found circulating in the blood, cerebrospinal fluid, and other tissues. This second stage of the illness, may vary in duration from 4 to 30 days or longer, and is of lesser severity than the septicemic stage. Meningitis, as reflected by a cerebrospinal fluid pleocytosis with or without meningeal signs and symptoms, is the primary feature of the immune stage. The severity of the meningitis varies considerably and does not correlate with the the severity of other clinical manifestations.[3] Leptospiruria is the rule during the immune stage of leptospirosis. It is of little significance and is unassociated with impaired renal function.[1] Unlike animal species, humans do not serve as a reservoir for the leptospire organisms. Excretion of leptospires by humans is a transient phenomenon, rarely occurring more than 5 to 6 weeks following the onset of disease. Human to human transmission via contamination by urine has not been reported.

In cases taking a favorable course, convalescence usually starts after 2 or 3 weeks, but full recovery may take a long time. The prognosis is largely dependent on the development of renal involvement and its treatment. Fatality

is low, but increases with advancing age and may reach 20% or more in patients with jaundice and kidney damage.[4] Immunity lasts for several years and is type specific. It, therefore, does not protect against simultaneous or later infections by other serotypes. Table 1 summarizes signs and symptoms reported in Louisiana cases, 1971 - 75.

The classical syndrome of Weil's disease is only exceptionally encountered. Less than 10% of reported cases of leptospirosis are icteric. This type of leptospirosis is distinctive in clinical expression but nonspecific with respect to serotype etiology. In addition to the signs and symptoms found in anicteric leptospirosis, Weil's disease is set apart by the presence of impaired renal and hepatic function, hemorrhage, vascular collapse, severe alterations in consciousness, and a high mortality rate.[1]

LABORATORY DIAGNOSIS

A variety of laboratory aids are available to help the clinician establish a diagnosis of leptospirosis. An understanding of the disease process of leptospirosis is required to select the cultural or serological test which will be of greatest value at each stage of the disease.

Laboratory confirmation of a case of leptospirosis may often prove difficult, even for facilities skilled in this area. A confirmed case of leptospirosis as defined by the U.S. Department of Health, Education and Welfare, is one which fulfills the following criteria: (1) a person with any clinical specimen which is cultured positive for leptospires, or (2) a person with clinical symptoms compatible with leptospirosis, such as the combination of fever, headache, jaundice, oliguria, and conjunctivitis, and either a seroconversion or a fourfold or greater rise in the microscopic agglutination(MA) titer between acute and convalescent serum specimens obtained 2 or more weeks apart and studied at the same laboratory.[2]

A presumptive case of leptospirosis is defined as a patient whose clinical symptoms are compatible with a diagnosis of leptospirosis and having either an MA titer of 1:100 or greater; or a positive macroscopic agglutination slide test (SA) reaction on a single serum specimen obtained after the onset of symptoms; or a stable MA titer of 1:100 or greater in 2 or more serum specimens obtained after the onset of symptoms.[1]

Isolation of organisms from any source has been difficult and infrequent. In their series, Heath, et al. report 14 isolations in 483 cases.[5] In the vast majority of cases, serologic tests were relied upon to establish a diagnosis. In general, serologic methods have been favored as being more practical and reliable. Unfortunately, there are no serologic tests which allow confirmation of a diagnosis of leptospirosis in less than 10 to 12 days after the onset of illness.

Leptospires may be isolated from cerebrospinal fluid or blood only during the first 8-10 days of clinical illness. Leptospires usually appear in the urine during the second week and may persist up to four weeks.[6] Demonstration of leptospiral organisms in various body fluids early in the course of the disease by means of specific stains or immunofluorescent techniques is not of sufficient reliability at this time and is not recommended as a routine laboratory procedure.[6]

The macroscopic slide agglutination test (SA), which utilizes killed or formalinized antigens, is probably the most rapid and useful screening test for human sera. The most widely used specific serologic test for leptrospirosis is the MA test; this MA test is time consuming and potentially hazardous to the laboratory technician but it is considered the reference test.

The SA test is most often used as a screening procedure to detect current infection. It can be performed rapidly and is designed to provide only serogroup specificity. The 12 standard antigens (prepared from 12 leptospiral strains representative of each of the serogroups known to be present in this country) are confined into 4 pools of 3 antigens each. When positive agglutination reactions occur upon addition of serum to one or more pools, the patient's serum is then tested separately against each antigen included in the pool.[6] If positive results are obtained, the titer and specific serotype are then determined by MA procedures.

The MA test also utilizes the 12 serogroups previously listed. This test is partially serotype-specific. Agglutinin elicited by leptospires of a particular serotype often agglutinate leptospires of other serotypes in the same or other serogroups. In principle, the serotype of an infecting strain can be determined with certainty only by isolation and cross-agglutination absorption studies. However, absorption studies on serum from an infected individual usually can indicate the infecting serotype with a high degree of accuracy.[6]

A new serologic test, the hemagglutination test (HA), is being used experimentally at the Center for Disease Control. It offers the advantage of detecting antibodies as early as the 4th day after the onset of illness. It is genus-

specific, requires only one antigen in the test system, and is less time consuming than the MA test.[1,6]

TREATMENT

In considering the pathogenesis of leptospirosis, it is apparent that to be of therapeutic benefit, an antimicrobial agent would have to be administered prior to the time that invading organisms produce damage to the endothelium of blood vessels and to various organs or tissues. It is well known that leptospires multiply rapidly and disseminate soon after invading the human host. Of greater importance, their initial effects may be reflected clinically late in the course of disease, and in many cases long after the invading organisms have disappeared from affected tissues. Although the necessity for prompt initiation of therapy has been repeatedly emphasized, it appears to be unrealistic to think that clinicians will entertain and establish a diagnosis of leptospirosis in time to initiate antimicrobial therapy prior to the occurrence of damage to tissues. A fundamental problem in evaluating the efficacy of any therapeutic regimen for this disorder is the fact that, in most cases, leptospirosis is a self-limited disease with a favorable course and outcome.

Reports on the value of antimicrobial treatment for human leptospirosis are very conflicting and have been based on single case reports or poorly controlled studies. Their application seems only to be beneficial when started on the first or second day of illness. Large doses seem to be required during a long period, including several days after symptoms have disappeared.

There is general agreement that penicillin or tetracycline therapy should be initiated if the diagnosis of leptospirosis is suspected early in the course of the disease, despite uncertainty with regards to their role in altering the course of the disease.[1]

The American Public Health Association currently recommends penicillin, streptomycin, erythromycin and tetracycline antibiotic therapy; these may be of value in the treatment of human leptospirosis when given early and in high dosage.[4] In case of renal failure, peritoneal or renal dialysis may be required.[4] In addition, special attention will have to be paid to fluid and electrolyte balance.

Despite the large number of antimicrobial agents available to the clinician, the therapeutic efficacy of any of these drugs for human leptospirosis remains in doubt. It appears that symptomatic and supportive care are still of primary importance in treatment.[1]

Table I

SIGNS AND SYMPTOMS OF CASES OF HUMAN LEPTOSPIROSIS REPORTED IN LOUISIANA, 1971 - 1975

SIGN AND SYMPTOMS	NUMBER OF CASES	PERCENT OF TOTAL*
Fever	10	43
Jaundice	10	43
Headache	0	39
Stiff Neck	8	35
Elevated CSF Protein	7	30
Elevated BUN	7	30
Albuminuria	5	22
Anuria/Oliguria	4	17
Hematuria	3	13
Chills	3	13
Nausea/Vomiting	2	9

* Total Cases - 23

PREVENTION

Sanitation measures can reduce the danger of spread of leptospirosis in both man and animals. Muddy farm areas should be drained and children should not be allowed barefoot on muddy soil. Control of the disease in the farm environment can be accomplished if the farmer practices closed herd techniques: segregation of the herd into groups, isolating new replacements for periods in excess of the known duration of the carrier state, and the elimination of environmental factors which would allow leptospiral infection from sylvatic sources or from neighboring farms.[7]

Control of leptospirosis in wild animals may be effected by trapping or by the use of poison; however, these methods have generally proved ineffective, especially with rodents. The ingenuity of the rodent may surpass that of the human who seeks to deny the rodent entrance to his dwelling. Moreover, the perseverance of rodents and their rapid rate of reproduction are sufficient to thwart most measures designed to control leptospirosis through control of the rodent population.[1]

Drinking water for humans as well as animals should be protected from contamination. Potentially contaminated waters should be identified and monitored accordingly. The public should be educated on the modes of transmission, avoidance of swimming or wading in potentially contaminated waters, and the need for proper protection when work requires such exposure.

Individuals who are employed in potentially hazardous occupations, such as rice workers, sugarcane field workers, dairy farmers, and abattoir workers should be properly warned of

the hazards inherent in their jobs and provisions made for their protection with boots and gloves.

General immunization of the population of the United States against leptospirosis would not appear to be justified, for the number of reported cases of leptospirosis appears to be low relative to the cost of producing and administering such a vaccine. Moreover, the efficacy and safety of leptospirosis vaccines have yet to be demonstrated conclusively.[1]

In addition to the use of hygienic practices for farm and pet animals, immunization may also be used to help prevent the disease, but not necessarily infection and renal shedding. Leptospire bacterins are available commercially and have been evaluated for safety and efficacy in laboratory animals and in domestic livestock. Vaccines are generally effective for about 6-9 months, and should represent the dominant local strains of the leptospire organism.

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MEASLES OUTBREAK IN ASSUMPTION PARISH

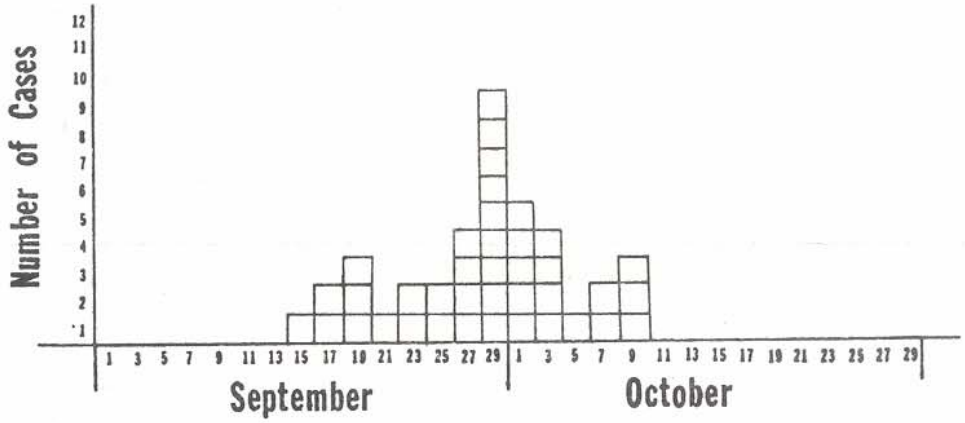
The Epidemiology staff of the Office of Health Services and Environmental Quality has been investigating an outbreak of measles (rubeola) centered in Assumption Parish. At least thirty nine cases have occurred in September and October. (See epidemic curve, Figure 1).

Of investigated cases to date, twenty eight are in Assumption Parish, ten are in St. Mary Parish, and one is in St. Martin Parish.

The Assumption Parish cases were mostly in school age children and were concentrated in the Pierre Part area, especially in the Pierre Part middle school. It is of interest that the adjoining elementary school, where the immunization level was close to 100%, had only three cases, at least two of whom had not been immunized. Overall, there was a history (not verified to date) of measles immunization in nine of the 28 Assumption Parish cases. The St. Mary Parish cases were younger, with five of ten occurring in pre-schoolers (Table 1). Only three of the ten cases gave a history of immunization (not verified to date).

Figure 1

Cases of measles in Pierre Part - Morgan City area by day of onset of rash



Many cases were classical presentations of rubeola. Temperature was recorded in 38 of the cases; in 37 of these it was greater than 102°F and in 20 of these it was greater than 104°. Of the 39 cases identified, a list of symptoms was obtained for 32. Cough was the most common, found in 23 cases. Photophobia or conjunctivitis was present in 14, coryza in 14, and sore throat in 13. Five cases had ear involvement. No other complications have been reported. There have been no deaths. Serological confirmation is available on two cases to date.

Control strategy is to define the extent of the outbreak and to create a wall of 100% immunity in the disease free borders of the involved areas. There is no evidence thus far of spread beyond the Assumption Parish - Morgan City area. Neighboring parishes are being asked to insure that their levels of immunization are as close to 100% as possible. In addition, campaigns are being carried out in the involved areas to vaccinate remaining susceptibles.

Epidemiological investigation and public health control was late because of delayed reporting of cases from the involved area. Doctors did not report cases and were reluctant to draw acute and convalescent sera. Not only is measles case reporting a legal requirement, it is essential for alerting public health officials to an outbreak so that control measures can be instituted. Measles serologies are also crucial for clarifying uncertain diagnoses as well as for documenting an outbreak.

Table 1

PARISH AND AGE DISTRIBUTION OF CASES

AGE	ASSUMPTION	ST. MARY	ST. MARTIN
<1	2	1	–
1–5	5	4	–
6–14	17	4	1
>14	4	1	–

SELECTED REPORTABLE DISEASES

(By Place of Residence)

STATE AND PARISH TOTALS REPORTED MORBIDITY September, 1976	ASEPTIC MENINGITIS	DIPHTHERIA	ENCEPHALITIS	ENCEPHALITIS, POST INFECTIOUS	HEPATITIS A AND UNSPECIFIED	HEPATITIS B	TUBERCULOSIS, PULMONARY	MENINGOCOCCAL INFECTIONS	PERTUSSIS	RABIES IN ANIMALS	RUBELLA*	SEVERE UNDERNUTRITION	SHIGELLOSIS	TYPHOID FEVER	OTHER SALMONELLOSIS	TETANUS	MEASLES	GONORRHEA	SYPHILIS, PRIMARY AND SECONDARY
TOTAL TO DATE 1975	119	0	24	10	422	143	377	32	47	5	284	12	111	4	180	4	1	16965	393
TOTAL TO DATE 1976	53	0	22	4	385	133	399	40	5	6	87	9	73	2	89	2	▲199	14428	447
TOTAL THIS MONTH	11	0	9	0	54	25	43	1	2	1	1	0	38	0	28	0	▲ 8	1779	61
ACADIA					1	1	1								1			21	1
ALLEN																		5	
ASCENSION																		3	
ASSUMPTION																	▲	3	
AVOYELLES					1		2											5	
BEAUREGARD			1															5	
BIENVILLE																		15	
BOSSIER			1							1			2		1			14	
CADDO					4	3	8						4		5			194	4
CALCASIEU						3							1		1			120	
CALDWELL																		1	
CAMERON																		2	
CATAHOULA																		2	
CLAIBORNE																		6	
CONCORDIA																		2	
DESOTO							1											12	
EAST BATON ROUGE			2		1		4								5		2	92	5
EAST CARROLL													1					9	
EAST FELICIANA																		1	
EVANGELINE						1													
FRANKLIN																		7	
GRANT																		4	
IBERIA																		15	1
IBERVILLE																		2	
JACKSON																			
JEFFERSON	1				8	4	3		1		1		3		1			86	11
JEFFERSON DAVIS							1											13	
LAFAYETTE																		43	
LAFOURCHE						1												21	2
LASALLE																			
LINCOLN					1													11	1
LIVINGSTON							1											6	
MADISON																		2	
MOREHOUSE							1											21	
NATCHITOCHES					2													12	
ORLEANS	7				13	9	8		1				22		10		6	601	17
OUACHITA					3		2											66	1
PLAQUEMINES																		2	
POINTE COUPEE																		3	1
RAPIDES					1													69	9
RED RIVER																		2	
RICHLAND			1															5	
SABINE							2											8	
ST. BERNARD					4	1									2			2	
ST. CHARLES	2						1											7	
ST. HELENA							1											7	
ST. JAMES																		2	
ST. JOHN			1		1													4	
ST. LANDRY					4	2	2								1			22	
ST. MARTIN					2												▲	5	
ST. MARY							1										▲	9	1
ST. TAMMANY			1										1					26	
TANGIPAHOA			2		2		1	1										19	1
TENSAS																		2	
TERREBONNE	1												4		1			2	1
UNION					1													7	
VERMILION							1											3	
VERNON					3													47	
WASHINGTON							2											19	2
WEBSTER					1													26	1
WEST BATON ROUGE																		12	
WEST CARROLL																		1	
WEST FELICIANA					1													38	2
WINN																		7	
OUT OF STATE																		1	

From January 1, through September 30, the following cases were also reported: 5-Brucellosis; 2-Leptospirosis; 1-Malaria contracted outside the U.S.A.

* Includes Rubella, Congenital Syndrome

▲ Additional cases occurring in Assumption, St. Mary, and St. Martin were not included in this report as official report cards have not yet been received by the Office of Statistics and Data Systems.